

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: McTigue et al.

Art Unit: NOT YET ASSIGNED

Serial No. NOT YET ASSIGNED

Examiner: NOT YET ASSIGNED

Filed: August 28, 3001

Atty. Docket: 0125-0016D2

For: Modifications of VEGF Receptor-2 Protein  
and Method of Use

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination of the above-identified application, Applicant herewith respectfully requests the following amendments:

IN THE CLAIMS:

Kindly delete claims 1-16 and replace with the following claims 17-27.

17. A method for identifying compounds which interact with the kinase domain of a modified RTK polypeptide comprising the steps of:

- (a) expressing in a host cell an isolated DNA sequence or variant thereof which encodes a modified RTK gene construct, wherein said RTK gene construct contains an RTK kinase domain  $\alpha$  helix D linked to RTK kinase domain  $\alpha$  helix E by a truncated RTK kinase insert domain (KID), said host cell capable of producing a modified RTK polypeptide that retains kinase activity and is suitable for x-ray crystallography; and
- (b) exposing said modified RTK polypeptide to said compound; and
- (c) evaluating the interaction between the kinase domain of said modified RTK polypeptide and said compound.

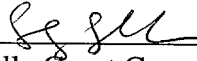
18. The method of claim 17, which further comprises:
  - (d) conducting said x-ray crystallography on said modified RTK polypeptide.
19. The method of claim 17 wherein said truncated kinase insert domain comprises a deletion of the highly charged residues from the KID.
20. The method of claim 17 wherein said truncated kinase insert domain comprises a deletion of 50 residues from the KID.
21. The method of claim 17 wherein said truncated kinase insert domain comprises a deletion of 60 residues from the KID.
22. The method of claim 17 wherein said truncated kinase domain linking said helix D to said  $\alpha$  helix E is of a sufficient length so as to allow said helices to maintain conformation associated with kinase structure.
23. The method of claim 17 wherein said RTK polypeptide is a member of the PDGFR family.
24. The method of claim 23 wherein said PDGFR member is selected from the group consisting of VEGFR-1, VEGFR-2, PDGFR- $\alpha$ , PDGFR- $\beta$ , stem cell growth factor receptor (c-kit), and colony stimulating factor-1 receptor (CSF-1R/c-fms).
25. The method of claim 17 wherein said RTK polypeptide is selected from the group consisting of insulin receptor (IRK), fibroblast growth factor receptor-1 (FGFR-1), and VEGFR-2.
26. The method of claim 17 wherein said RTK polypeptide is VEGFR-2.
27. The method of claim 17 wherein said modified RTK polypeptide comprises the VEGFR2 $\Delta$ 50 polypeptide of SEQ ID NO: 5.

REMARKS

It is respectfully requested that the Examiner enter these amendments prior to examining the application on its merits.

Respectfully submitted,

SHANKS & HERBERT

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